Tuberculosis

George Orwell, Franz Kafka, Charlotte Brontë and Frederic Chopin all had something in common—they all died of a disease known, at the time, as consumption. This year marks the 125th anniversary of the discovery, by Robert Koch, of *Mycobacterium tuberculosis*, the infectious agent of the disease we now call TB. The word 'consumption' conjures images of bygone eras, but the word 'tuberculosis' is synonymous with immense present-day mortality and suffering, largely in developing countries, where HIV and TB coinfection form a lethal combination (see News, page 268).

More than one-third of the world's population is infected with tubercle bacilli. One in every ten of these individuals will develop TB at some point in their lifetime, and this year around 1.7 million people will die of the disease.

Fifty years ago it seemed as though TB would soon be consigned to the pages of history. The development of the antibiotic streptomycin allowed, for the first time, those with TB to be cured. And for a short while the disease seemed on the ebb. Today, however, TB remains as much of a threat as it was in the preantibiotic era. So what happened? Poor adherence to TB control programs, the consequent emergence of drug resistance, and the widespread prevalence of HIV has caused a resurgence in the incidence of the disease, which threatens to escalate further out of control. New drugs, better vaccines and new diagnostics are desperately needed to turn the tide of infection (see News, pages 266, 267 and 274).

One hundred twenty-five years after the discovery of *M. tuberculosis*, how much do we understand about the pathogen that remains one of the world's major infectious killers? Is it feasible to imagine that we might bring TB back under control? And if so, how far are we from this goal? What are the scientific, logistical and financial obstacles to developing and introducing more effective therapies for TB?

To find the answers to some of these questions, we polled approximately 50 leading TB experts and asked them to select papers that they felt had provided the most important advances in tuberculosis research over the past three years. Their insight was illuminating and encouraging (see page 276). Although progress toward developing more effective vaccines for TB has been modest, the recent identification and development of several new drugs offers real hope that new antibiotics could shorten the current six-month treatment time and reduce the emergence of drug resistance. This is a remarkable achievement in today's climate of languishing investment in development of new antimicrobials.

Soberingly, however, Susan Dorman and Richard Chaisson note that the specter of extensively drug-resistant tuberculosis (XDR-TB)—bacteria resistant to first and second-line drugs—has become a grim reality (see page 295). More new drugs are needed and a combination of several new antibiotics with different mechanisms of action will be needed to curb the spread of XDR-TB and tackle latent disease.

What are the challenges to developing and deploying new drugs? As Ann Ginsberg and Melvin Spigelman explain, understanding the biological mechanisms of persistence and latency will be key, as will developing better animal models that reliably predict the duration of treatment in humans so that effective drug combinations can be quickly identified (see page 290). It is encouraging, therefore, that several papers selected by our sample of experts have furthered our understanding of persistence and latency. These papers, and those providing other notable advances, are placed in context in the News and Views articles on pages 279-287.

What has fueled the boost to tuberculosis research? Stefan Kaufmann and Shreemanta Parida discuss how sources of funding for TB research have changed over the past decades and how these changing patterns of funding have influenced the pace and nature of research (see page 299). Investment in TB research today will not translate to improved control for at least another decade, so it is crucial that funding for TB continue to increase.

But it is not sufficient to increase funding for basic TB research. Radical changes need to be made to the system by which drugs and vaccines are marketed and distributed. As noted in the market analysis on page 309, from a commercial perspective, there is presently little financial incentive for pharmaceutical companies to invest in drug development for diseases that, like TB, mostly affect populations that cannot afford necessary medicines. In a Commentary on page 304, Carl Nathan provides some ideas for how the system of drug development should be reformed to ensure that new medicines reach populations that need them most.

We hope that the articles in this special focus on tuberculosis will provoke thought and discussion and we encourage our readers to share their opinions with us. We sincerely appreciate the financial support of AstraZeneca, Johnson & Johnson PRD and Tibotec in producing this focus. *Nature Medicine* takes full editorial responsibility for the content of these pages.